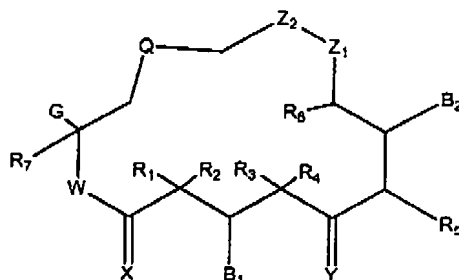


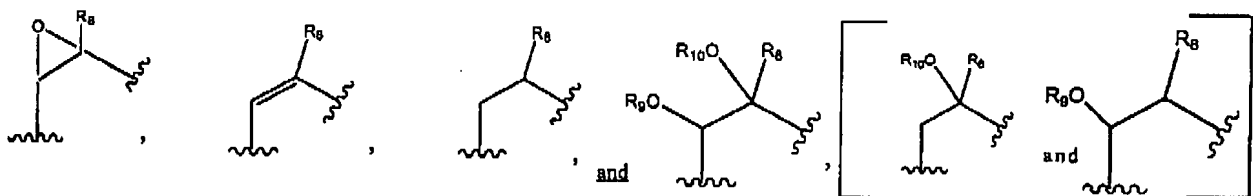
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1. (Thrice amended) A compound of the formula

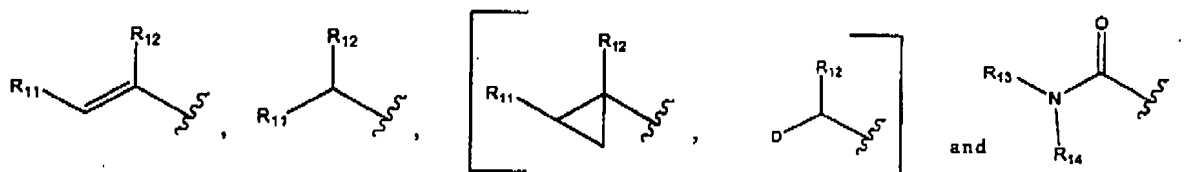


V

Q is selected from the group consisting of



G is selected from the group consisting of alkyl[.]; substituted alkyl[.]; substituted aryl[.]; a 4 to 7 membered monocyclic, 7 to 11 membered bicyclic, or 10 to 15 membered tricyclic ring system having between 1 and 3 heteroatoms selected from nitrogen, oxygen, and sulfur; [heterocyclo,]



X is O or H, H;

Y is selected from the group consisting of O; H, OR₁₆; OR₁₇, OR₁₇; NOR₁₈; H, NOR₁₉; H, NR₂₀R₂₁; H, H; and CHR₂₂; wherein OR_{17a}, OR₁₇ can be a cyclic ketal;

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Z_1 and Z_2 are independently [selected from the group consisting of] CH_2 , O, NR_{23} , S, and SO_2 , wherein only one of Z_1 and Z_2 can be heteroatom];

B_1 and B_2 are independently selected from the group consisting of OR_{24} , OCOR_{25} , and $\text{O-C(=O)-NR}_{26}\text{R}_{27}$, and when B_1 is H and Y is OH, H, they can form a six-membered ring ketal or acetal;

[D is selected from the group consisting of $\text{NR}_{28}\text{R}_{29}$, $\text{NR}_{30}\text{COR}_{31}$ and saturated heterocycle;]

R_1 , R_2 , R_3 , R_4 , R_5 , R_7 , R_{13} , R_{14} , R_{18} , R_{19} , R_{20} , R_{21} , R_{22} , R_{26} and R_{27} are selected from the group consisting of H, alkyl, substituted alkyl, and aryl, and when R_1 and R_2 are alkyl can be joined to form a cycloalkyl, and when R_3 and R_4 are alkyl can be joined to form a cycloalkyl;

R_6 is methyl;

R_9 , R_{10} , R_{16} , R_{17} , R_{24} , R_{25} and R_{31} are selected from the group consisting of H, alkyl, and substituted alkyl;

R_{11} , R_{12} , R_{28} , R_{30} , R_{32} , and R_{33} are selected from the group consisting of H, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl and heterocycle;

R_8 is hydrogen or methyl;

R_{15} , R_{23} and R_{29} are selected from the group consisting of H, alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, heterocycle, $\text{R}_{32}\text{C=O}$, R_{33}SO_2 , hydroxy, O-alkyl or O-substituted alkyl; and

the pharmaceutically acceptable salts thereof and any hydrates, solvates or geometric, optical and stereoisomers thereof;

with the proviso that compounds wherein

W and X are both O; and

R_1 , R_2 and R_7 are H; and

R_3 , R_4 and R_6 are methyl; and

R_8 is H or methyl; and

[Z_1 and Z_2 are CH_2 ; and]

G is 1-methyl-2-(substituted-4-thiazolyl)ethenyl; and

Q is as defined above

are excluded.

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2. The compound of claim 1 wherein

Q is



X is O;

Y is O;

Z₁, and Z₂, are CH₂ and

W is NR₁₅.

3. A compound selected from the group consisting of:

[1S-[1R*,3R*(E),7R*,10S*,11R*,12R*,16S*]]-7,11-Dihydroxy-8,8,10,12,16-pentamethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4,13,17-trioxabicyclo[14.1.0]heptadecane-5,9-dione;

[1S-[1R*,3R*(E),7R*,10S*,11R*,12R*,16S*]]-7,11-Dihydroxy-8,8,10,12-tetramethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4,13,17-trioxabicyclo[14.1.0]heptadecane-5,9-dione;

[4S-[4R*,7S*,8R*,9R*,15R*(E)]]-4,8-Dihydroxy-5,5,7,9,13-pentamethyl-16-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-1,10-dioxa-13-cyclohexadecene-2,6-dione;

[4S-(4R*,7S*,8R*,9R*,15R*(E)]]-4,8-Dihydroxy-5,5,7,9-tetramethyl-16-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-1,10-dioxa-13-cyclohexadecene-2,6-dione;

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[1S-[1R*,3R*(E),7R*,10S*,11R*,12R*,16S*]]-7,11-Dihydroxy-8,8,10,12,16-pentamethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4,14,17-trioxabicyclo[14.1.0]heptadecane-5,9-dione;

[1S-[1R*,3R*(E),7R*,10S*,11R*,12R*,16S*]]-7,11-Dihydroxy-8,8,10,12,-tetramethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4,14,17-trioxabicyclo[14.1.0]heptadecane-5,9-dione;

[4S-[4R*,7S*,8R*,9R*,15R*(E)]]-4,8-Dihydroxy-5,5,7,9,13-pentamethyl-16-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-1,11-dioxa-13-cyclohexadecene-2,6-dione;

[4S-[4R*,7S*,8R*,9R*,15R*(E)]]-4,8-Dihydroxy-5,5,7,9,13-tetramethyl-16-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-1,11-dioxa-13-cyclohexadecene-2,6-dione;

[1S-[1R*,3R*(E),7R*,10S*,11R*,12R*,16S*1]]-7,11-Dihydroxy-8,8,10,12,16-pentamethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4,17-dioxabicyclo[14.1.0]heptadecane-9-dione;

[1S-[1R*,3R*(E),7R*,10S*,11R*,12R*,16S*1]]-7,11-Dihydroxy-8,8,10,12,tetramethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4,17-dioxabicyclo[14.1.0]heptadecane-9-dione;

[1S-[1R*,3R*(E),7R*,10S*,11R*,12R*,16S*1]]-7,11-Dihydroxy-3,8,8,10,12,16-hexamethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione;

[1S-[1R*,3R*(E),7R*,10S*,11R*,12R*,16S*1]]-7,11-Dihydroxy-3,8,8,10,12-pentamethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione;

[4S-[4R*,7S*,8R*,9R*,15R*(E)]]-4,8-Dihydroxy-5,5,7,9,13,16-hexamethyl-16-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-1-oxa-13-cyclohexadecene-2,6-dione;

[4S-[4R*,7S*,8R*,9R*,15R*(E)]]-4,8-Dihydroxy-5,5,7,9,16-pentamethyl-16-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-1-oxa-13-cyclohexadecene-2,6-dione;

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[1S-[1R*,3R*(B),7R*,10S*,11R*,12R*,16S*1]-7,11-Dihydroxy-8,8,10,12,16-pentamethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione;

[1S-[1R*,3R*(E),7R*,10S*,11R*,12R*,16S*]]-7,11-Dihydroxy-6,8,8,10,12-pentamethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione;

[1S-[1R*,3R*(E),7R*,10S*,11R*,12R*,16S*]]-7,11-Dihydroxy-8,8,10,12,16-pentamethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4-aza-17-oxabicyclo[14.1.0]heptadecane-5,9-dione;

[1S-[1R*,3R*(E),7R*,10S*,11R*,12R*,16S*]]-7,11-Dihydroxy-8,8,10,12-tetramethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4-aza-17-oxabicyclo[14.1.0]heptadecane-5,9-dione;

[4S-[4R*,7S*,8R*,9R*,15R*(E)]]-4,8-Dihydroxy-5,5,7,9,13-pentamethyl-16-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-1-aza-13-cyclohexadecene-2,6-dione;

[4S-[4R*,7S*,8R*,9R*,15R*(E)]]-4,8-Dihydroxy-5,5,7,9-tetramethyl-16-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-1-aza-13-cyclohexadecene-2,6-dione;

[1S-[1R*,3R*(E),7R*,10S*,11R*,12R*,16S*]]-7,11-Dihydroxy-4,8,8,10,12,16-hexamethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4-aza-17-oxabicyclo[14.1.0]heptadecane-5,9-dione;

[1S-(1R*,3R*(E),7R*,10S*,11R*,12R*,16S*)]-7,11-Dihydroxy-4,8,8,10,12-pentamethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-4-aza-17-oxabicyclo[4.10]heptadecane-5,9-dione;

[4S-[4R*-7S*,8R*,*9R-,15R*(E)]]-4,8-Dihydroxy-1,5,5,7,9,13-hexamethyl-16-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-1-aza-13-cyclohexadecene-2,6-dione;

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[4S-[4R*,7S*,8R*,9R*,15R*(E)]-4,8-Dihydroxy-1,5,5,7,9-pentamethyl-16-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-1-aza-13-cyclohexadecene-2,6-dione;

[1S-[1R*,3R*(E),7R*,10S*,11R*,12R*,16S*]-7,11-Dihydroxy-8,8,10,12,16-pentamethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-aza-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione;

[1S-[1R*,3R*(E),7R*,10S*,11R*,12R*,16S*]-7,11-Dihydroxy-8,8,10,12-tetramethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-13-aza-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione;

[4S-[4R*,7S*,8R*,9R*,15R*(E)]-4,8-Dihydroxy-5,5,7,9,13-pentamethyl-16-(1-methyl-2-(2-methyl-4-thiazolyl)ethenyl)-10-aza-1-oxa-13-cyclohexadecene-2,6-dione;

[4S-[4R*,7S*,8R*,9R*,15R*(E)]-4,8-Dihydroxy-5,5,7,9-tetramethyl-16-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-10-aza-1-oxa-13-cyclohexadecene-2,6-dione;

[1S-[1R*,3R*(E),7R*,10S*,11R*,12R*,16S*]-7,11-Dihydroxy-8,8,10,12,16-pentamethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-14-aza-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione;

[1S-[1R*,3R*(E),7R*,10S*,11R*,12R*,16S*]-7,11-Dihydroxy-8,8,10,12-tetramethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-14-aza-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione;

[4S-[4R*,7S*,8R*,9R*,15R*(E)]-4,8-Dihydroxy-5,5,7,9,13-pentamethyl-16-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-11-aza-1-oxa-13-cyclohexadecene-2,6-dione;

[4S-[4R*,7S*,8R*,9R*,(E)]-4,8-Dihydroxy-5,5,7,9-tetramethyl-16-[1-methyl-2-(2-methyl-4-thiazolyl)ethenyl]-11-aza-1-oxa-13-cyclohexadecene-2,6-dione;

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[1S-[1R*,3R*,7R*,10S*,11R*,12R*,16S*]]-N-Phenyl-7,11-dihydroxy-8,8,10,12,16-pentamethyl-5,9-dioxo-4,17-dioxabicyclo[14.1.0]heptadecane-3-carboxamide;

[1S-[1R*,3R*,7R*,10S*,11R*,12R*,16S*]]-N-Phenyl-7,11-dihydroxy-8,8,10,12-tetramethyl-5,9-dioxo-4,17-dioxabicyclo[14.1.0]heptadecane-3-carboxamide;

[4S-[4R*,7S*,8R*,9R*,15*]]-N-Phenyl-4,8-dihydroxy-5,5,7,9,13-pentamethyl-2,6-dioxo-1-oxa-13-cyclohexadecene-16-carboxamide;

[4S-[4R*,7S*,8R*,9R*,15R*]]-N-Phenyl-4,8-dihydroxy-5,5,7,9-tetramethyl-2,6-dioxo-1-oxa-13-cyclohexadecene-16-carboxamide;

[1S-[1R*,3R*(E),7R*,10S*,11R*,12R*,16S*]]-7,11-Dihydroxy-8,8,10,12,16-pentamethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)cyclopropyl]-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione;

[1S-[1R*,3R*(E),7R*,10S*,11R*,12R*,16S*]]-7,11-Dihydroxy-8,8,10,12-tetramethyl-3-[1-methyl-2-(2-methyl-4-thiazolyl)cyclopropyl]-4,17-dioxabicyclo[14.1.0]heptadecane-5,9-dione;

[4S-[4R*,7S*,8R*,9R*,15R*(E)]]-4,8-Dihydroxy-5,5,7,9,13-pentamethyl-16-[1-methyl-2-(2-hydroxymethyl-4-thiazolyl)ethenyl]-1-aza-13(Z)-cyclohexadecene-2,6-dione;
and the pharmaceutically acceptable salts, solvates and hydrates thereof.

4. (Thrice amended) A method of treating breast cancer, ovary cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 1.

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Canceled 5. (Twice amended) A method of treating hyperproliferative cellular disease in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 1.

Canceled 6. (Twice amended) A method of treating a disease associated with angiogenesis in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 1.

7. (New) The method of claim 4, wherein the cancer is cancer [carcinoma] of the breast, ovary, or colon.

8. (New) A method of treating breast cancer, ovary cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 2.

Canceled 9. A method of treating hyperproliferative cellular disease in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 2.

Canceled 10. A method of treating a disease associated with angiogenesis in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 2.

11. (Amended) A method of treating breast cancer, ovary cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 3.

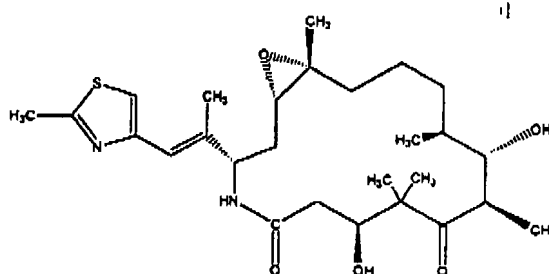
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Canceled 12. A method of treating hyperproliferative cellular disease in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 3.

Canceled 13. A method of treating a disease associated with angiogenesis in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 3.

14. The compound of claim 1 having the formula:



or a pharmaceutically acceptable salt, hydrate, solvate, geometrical isomer, optical isomer, or stereoisomer thereof.

15. (New) A method of treating breast cancer, ovary cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 14.

16. (New) The method of claim 15, wherein the cancer is cancer of the breast, ovary, or colon.

17. (New) The method of claim 8, wherein the cancer is cancer of the breast, ovary, or colon.

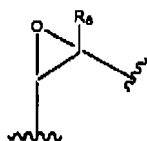
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18. (New) The method of claim 11, wherein the cancer is cancer of the breast, ovary, or colon.

19. (New) The compound of claim 1, wherein G is 1-methyl-2-(substituted-4-thiazolyl) ethenyl group.

20. (New) The compound of claim 1, wherein Q is



21. (New) The compound of claim 1, wherein W is NR₁₅.

22. (New) The compound of claim 1, wherein X and Y are each O.

23. (New) A method of treating breast cancer, ovary cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 19.

24. (New) The method of claim 23, wherein the cancer is cancer of the breast, ovary, or colon.

25. (New) A method of treating breast cancer, ovary cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 20.

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26. (New) The method of claim 25, wherein the cancer is cancer of the breast, ovary, or colon.

27. (New) A method of treating breast cancer, ovary cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 21.

28. (New) The method of claim 27, wherein the cancer is cancer of the breast, ovary, or colon.

29. (New) A method of treating breast cancer, ovary cancer, colon cancer, head and neck cancer, lung cancer, gynecological cancers, brain cancer, germ cell cancer, urothelial cancer, esophageal cancer, prostate cancer, bladder cancer, or pancreatic cancer in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 22.

30. (New) The method of claim 29, wherein the cancer is cancer of the breast, ovary, or colon.

31. (New) A method of treating a cancer responsive to microtubule stabilization in a patient comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 1.

32. (New) A method of treating a cancer responsive to microtubule stabilization in a patient comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 2.

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33. (New) A method of treating a cancer responsive to microtubule stabilization in a patient comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 3.

34. (New) A method of treating a cancer responsive to microtubule stabilization in a patient comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 14.

35. (New) A method of treating a cancer responsive to microtubule stabilization in a patient comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 19.

36. (New) A method of treating a cancer responsive to microtubule stabilization in a patient comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 20.

37. (New) A method of treating a cancer responsive to microtubule stabilization in a patient comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 21.

38. (New) A method of treating a cancer responsive to microtubule stabilization in a patient comprising administering to a patient in need of such treatment a therapeutically effective amount of a compound of claim 22.

39. (New) The method of claim 4, further comprising administering one or more of a second anti-cancer agent.

40. (New) The method of claim 39, wherein the second anti-cancer agent acts in a phase of the cell cycle other than the G₂-M phase.

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41. (New) The method of claim 40, wherein the second anti-cancer is a thymidilate synthase inhibitor, a DNA cross linking agent, a topoisomerase I or II inhibitor, a DNA alkylating agent, a ribonuclease reductase inhibitor, a cytotoxic factor, or a growth factor inhibitor.
42. (New) The method of claim 4, further comprising administering radiation therapy.
43. (New) A pharmaceutical composition comprising the compound of claim 1 and a pharmaceutically acceptable vehicle or diluent.
44. (New) A pharmaceutical composition comprising the compound of claim 2 and a pharmaceutically acceptable vehicle or diluent.
45. (New) A pharmaceutical composition comprising the compound of claim 3 and a pharmaceutically acceptable vehicle or diluent.
46. (New) A pharmaceutical composition comprising the compound of claim 14 and a pharmaceutically acceptable vehicle or diluent.
47. (New) A pharmaceutical composition comprising the compound of claim 19 and a pharmaceutically acceptable vehicle or diluent.
48. (New) A pharmaceutical composition comprising the compound of claim 20 and a pharmaceutically acceptable vehicle or diluent.
49. (New) A pharmaceutical composition comprising the compound of claim 21 and a pharmaceutically acceptable vehicle or diluent.
50. (New) A pharmaceutical composition comprising the compound of claim 22 and a pharmaceutically acceptable vehicle or diluent.

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51. (New) A method of treating melanoma, non-Hodgkin's lymphoma, multiple myeloma, or Kaposi's sarcoma in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 1.

52. (New) A method of treating melanoma, non-Hodgkin's lymphoma, multiple myeloma, or Kaposi's sarcoma in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 2.

53. (New) A method of treating melanoma, non-Hodgkin's lymphoma, multiple myeloma, or Kaposi's sarcoma in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 3.

54. (New) A method of treating melanoma, non-Hodgkin's lymphoma, multiple myeloma, or Kaposi's sarcoma in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 14.

55. (New) A method of treating melanoma, non-Hodgkin's lymphoma, multiple myeloma, or Kaposi's sarcoma in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 19.

56. (New) A method of treating melanoma, non-Hodgkin's lymphoma, multiple myeloma, or Kaposi's sarcoma in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 20.

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57. (New) A method of treating melanoma, non-Hodgkin's lymphoma, multiple myeloma, or Karposi's sarcoma in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 21.

58. (New) A method of treating melanoma, non-Hodgkin's lymphoma, multiple myeloma, or Karposi's sarcoma in a patient in need of said treatment which comprises administering to said patient a therapeutically effective amount of a compound of claim 22.